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14. ABSTRACT

Our intent has been to identify African American males diagnosed with prostate cancer between the ages of 40 and 75 and to enter them along with their at risk relatives into a program of cancer education, cancer screening, and early intervention to reduce disparities in prostate cancer incidence and mortality rates in the African American community in Nebraska and Mississippi. Family history of prostate and other cancers is being recorded with the purpose of identifying any hereditary prostate cancer syndrome. In addition, social and behavioral determinants are collected and recorded during the interview process for the final analysis. This will be possible through the recruitment of a total of 800 African Americans who have been diagnosed with prostate cancer, through recruitment activities and screenings in Omaha, Nebraska, and Jackson, Mississippi.

15. SUBJECT TERMS

Nothing listed

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Introduction

Our intent has been to identify African American males diagnosed with prostate cancer between the ages of 40 and 75 and to enter them along with their at risk relatives into a program of cancer education, cancer screening, and early intervention to reduce disparities in prostate cancer incidence and mortality rates in the African American community in Nebraska and Mississippi. Family history of prostate and other cancers is being recorded with the purpose of identifying any hereditary prostate cancer syndrome. In addition, social and behavioral determinants are collected and recorded during the interview process for the final analysis. This will be possible through the recruitment of a total of 800 African Americans who have been diagnosed with prostate cancer, through recruitment activities and screenings in Omaha, Nebraska, and Jackson, Mississippi.

Keywords

Prostate cancer, familial cancer, African American, participant recruitment, database

Body/Accomplishments

Task 1: Participant Identification and Access (Years 1- 3)

At Creighton University, recruitment of subjects has been through cooperation with local urologists as well as through promotion to the community by study personnel's appearance on two local television programs that target the African American community, Real Talk and Healthy Choices on Omaha CTI22; attendance at local health fairs; publication of an article about the study in *Omaha Star* newspaper serving the Omaha African American community; an announcement of the study emailed to all online subscribers of the *Omaha World Herald* newspaper; an advertisement on the study emailed to all Creighton University physicians in their monthly School of Medicine newsletter; creation of a billboard to be displayed in an area close to North East Omaha where over 90% of African Americans reside throughout September 2012; compilation of lists of church leaders and secretaries and neighborhood watch leaders received an email or written study invitations to share with their communities; and multiple barber shop blitz was held in 2013 wherein local barbers agreed to speak to each of their clients about prostate cancer and informed them of our study and to contact our team if interested in participating. Recruitment in Mississippi was done in collaboration with a local African American urologist through his clinic database. (Table 1)

One-hundred and twenty-five participants were identified at Creighton who met the eligibility criteria. Twenty-six of these participants have been interviewed and data collected from the interviews has been entered into the study-specific database according to protocol. DNA has been collected and stored according to protocol for those eligible participants who have agreed. The remaining potential participants have received a letter introducing the study and informing them that the project coordinator will be contacting them regarding participation.

Five-hundred and thirty-seven participants were identified in Jackson, Mississippi who met the eligibility criteria. Sixty-seven of these participants have been interviewed and data collected from the interviews and has been entered into the study-specific database. Blood samples has been collected and stored at Creighton for thirty-seven subjects. The remaining individuals have either refused participation after their interviews or were not selected for blood draw because there was no indication of familial prostate cancer. (Table 2)

Task 2: Data Collection and Management (Years 1- 3)

The study-specific database has been constructed, including onscreen instructions for its use. As stated above, data collection has been completed at Creighton and Jackson State University.

The database variables on social and behavioral determinants and risk exposure pathways suggested by the community partners were added to the database with appropriate quality controls incorporated into the program. (Figures 1 and 2)

Task 3. Prostate Cancer Prevention and Health Education and Referral (Years 1.5-3)
Screening interviews are ongoing at both study sites, with participants positive for prostate cancer family history being identified and receiving appropriate education, genetic counseling, and/or referral. During each interview the research coordinator identifies at risk family members and encourages the participant to discuss their risk with them as well as our screening recommendations. The participant was also asked to have the family member call the research coordinator directly to discuss their risk and the recommendations. The Jackson State University team developed and gave a presentation to a prostate cancer support group at their meeting on July 19, 2011. This presentation has been shared with the Creighton University Community Engagement Team. The CU project coordinator has attended three health fairs in the community to provide awareness of prostate cancer and recruitment material for the study. (Figure 3)

Task 4 Biostatistical Analysis
The age range of the participants, all of whom were affected with prostate cancer, was between 44 and 90, with a mean age of 71. Both the familial and the nonfamilial cases had a mean age of 71. The JSU participants were older than the CU participants on average. The JSU participants had a mean age of 72.9 (sd = 7.25, range: 58 to 90) and the CU participants had a mean age of 65.4 (sd = 8.16, range: 44 to 77). Likewise, the JSU participants had an older age of diagnosis. The JSU participants (N=67) had a mean age at diagnosis of 62.8 (sd = 8.2, range: 40 to 79) and the CU participants (N=25 after one sibling from a sib pair was dropped from analysis) had a mean age at diagnosis of 59.5 (sd=8.3, range: 41 to 73).

Using the presence of affected 1st degree relatives and nephews as the criteria for familiality, JSU had 45% participants with familial prostate cancer and CU had 40%. However, the JSU pedigree information tended to be more extensive; thus, allowing affected cousins to be added to the criterion increased the proportion of familial prostate cancer in the JSU families to 54%, while the familiality estimate in the CU families remained at 40%. With either definition of familiality, the proportions were not statistically different across the two study sites. Using a chi-square statistic and the first definition of familiality, the p-value was 0.68 and using the second definition (including cousins), the p-value was 0.24. Similarly, the Kaplan-Meier plots in figures 4 and 5 show no significant difference in age of diagnosis between the familial and non-familial cases using either definition of familiality and combined study site data.

Looking at the JSU data separately, a Kaplan-Meier plot shows no significant difference in the age of onset between the familial and non-familial cases (p= 0.52 using the log-rank test) (figure 6). At this study site, there does seem to be a trend, contrary to what one might expect, that the familial cases had later ages of diagnosis. Familiality was defined as having a first degree relative or a nephew with PrCa. Altering the definition of familiality to include affected cousins and uncles also resulted in no significant difference between the age of onset between familial and non-familial cases (p=0.97). Among the CU participants, the Kaplan-Meyer plot shows suggestive evidence of a difference age of onset between the familial and non-familial cases (p=0.09 using the log-rank test), with familial cases having earlier age at diagnosis (figure 7).

We also assessed a more stringent definition of familiality which requires 2 first degree relatives to be affected in addition to an affected individual for the family to be considered familial. With this stricter definition, 19.6% of the families in this study have familial prostate cancer, which is still higher than

the 10-15% that we expected [Mandal et al., 2008; Zeegers et al., 2003]. 17.9% and 24% of the JSU and CU families, respectively, met this definition and the percentages were not significantly different. Looking at both sites together in Kaplan-Meier plots, contrary to what we would expect from the literature, the (strict) familial cases did not have earlier ages of diagnosis (p-value = 0.62). There was no difference between the familial and non-familial ages of diagnosis among the JSU families (log rank p-value = 0.96, N=67) but there does appear to be a difference after age 45 among the CU families (N=25), with earlier ages of diagnosis among the familial cases. However, the earliest ages of diagnosis in the CU group occurred in non-familial cases, so again the log-rank p-value is non-significant at a 0.05 alpha level (p=0.14, figure 8).

The number of variables in the study was large compared to the number of study participants. Thus, as a data reduction technique, variables that were considered to be related were together combined into principle components. Three sets of psychosocial variables, exposure variables, health/health behavior variables, neighborhood variables, and variables relating to current and childhood socioeconomic status were combined into seven sets of principle components. These were in turn analyzed using the generalized linear modeling selection procedure (GLMSELECT) in SAS. The significant factors were assessed and the original variables within these factors were selected if the absolute value of the loading was 0.3 or higher. (Table 3)

With age at diagnosis as the dependent variable, the best regression model included diabetes (borderline significant with a p-value of 0.05), exposure to contaminated water at one's residence at some point in life (p-value = 0.04), the psychosocial factor of talking to their mother regarding prostate cancer as a coping skill (p-value = 0.001), and expressed level of feelings of embarrassment about talking with their doctor (p-value = 0.006).

12% of the CU participants talked with their mother compared to only 3% of the JSU participants, who were older, on average. Thus age is likely a driving factor for the significance of this variable, which is negatively correlated with age at onset, because the mothers of older participants would have passed on. The high statistical significance of this variable may simply be a function of age. Or, it could be that talking to one's mother may predispose one to earlier screening for prostate cancer.

Exposure to contaminated water is also negatively correlated with age at onset – i.e., those who stated they were exposed to contaminated water in their homes were more likely to have earlier ages of onset. 20% of the CU participants stated that they had been exposed to contaminated water, versus only 3% of the JSU participants. Although living in a rural area is not significantly correlated with age at diagnosis (rho=0.13, p-value= 0.23, N=92), the JSU participants were more likely to have grown up in rural areas than the CU participants (rho=0.20, p-value= 0.05, N=92), and this might be an explanation for the difference in (known) exposure to contaminated drinking water.

The prevalence of diabetes among the participants at the two study sites was quite similar, with 40% at CU and 34% at JSU. The scores for the question on feelings of embarrassment with the doctor (EmbDoc) were similar, slightly higher at CU (4.72 vs. 4.49 at JSU), indicating that most did not feel embarrassed to talk with their doctor.

High scores on the EmbDoc question indicated strong disagreement. All men who were diagnosed under the age of 50 disagreed very strongly, indicating that none of the men in this group were embarrassed to talk with their doctor, while one of the most elderly men agreed very strongly. The responses to this question were also negatively correlated with age at the time of the questionnaire (rho= -0.28, p-value = 0.009), which is also correlated with the age of diagnosis (rho= 0.68, p-value < 0.0001). As a group, the younger men felt more comfortable talking with their doctor and it is likely that the age and the corresponding attitudes of the age group are reflected in the significance of this

variable in explaining the variance in the age of diagnosis; that is, that the attitude itself may not be a driver in the age of diagnosis.

The prevalence of diabetes at both sites was surprisingly high. In a CDC report, the prevalence rate in 2011 for Black men ages 45 to 65 was 17.6%. For this age group, the rate was 37.5% at the CU site (N=8) and 57.1% at the JSU site (N=7) with a combined rate of 46.7%, 2.65 times higher than the CDC estimate. In the same CDC report, the rate for Black men ages 65 to 74 was 30.7% in 2011. At CU in this age group, the rate was 54.5% (N=11) and at JSU it was 24.2% (N=8) with a combined rate of 31.8%; the age group of 65 to 74 in our study was more in line with the 2011 CDC estimate. These rates in our sample were also surprising in light of a 2011 study of U.S. Veterans that reported that both black and white men with diabetes had reduced risk of having prostate cancer than those without diabetes (RR = 0.89, 95%CI = 0.87-0.91) [Atchison et al., 2011]. In contrast, another 2011 paper noting the high prevalence of both diabetes and prostate cancer among Black men showed that the diagnosis of diabetes mellitus was significantly associated with more aggressive prostate cancer (Gleason scores of 8-10), independent of Black race [Mitin et al., 2011].

An analysis of racial/ethnic differences in lifestyle-related factors and prostate cancer risk in the Multiethnic Cohort Study (N=75,216) did not find education, physical activity, BMI or alcohol intake to be significant factors for prostate cancer risk. Park et al. (2015) did find current smoking and history of diabetes were found to be associated with prostate cancer risk (but appear to be protective, with relative risks of 0.72 and 0.78, respectively). We did not find education, physical activity at any age, alcohol, smoking or living with a smoker to be associated with age at diagnosis in this study. Park et al concluded that underlying genetic factors may explain prostate cancer risk rather than lifestyle factors.

Diabetes is a component of metabolic syndrome, in which dysregulation of levels of hormones such as testosterone and adipokines such as leptin and adiponectin have been shown to be associated with the aggressiveness of prostate cancer. The prostate is itself an endocrine organ. Obesity, hypercholesterolemia and hyperinsulinemia as well as diabetes have been shown implicated in the development and/or the progression of prostate cancer [Rhee et al., 2015]. A metaanalysis of studies of metformin treatment for diabetes among men with prostate cancer showed an improvement in overall survival [Stopsack et al., 2015]. Hence, the association we see in our study between age of diagnosis (of prostate cancer) and diabetes mellitus is biologically plausible.

Along this vein, Nemesure et al. (2014) showed a two-fold increase in risk of prostate cancer among men in the top quartile of a measure of central adiposity (waist to hip ratio) versus those in the bottom quartile in a Black population in Barbados (963 cases and 941 controls). In the same study, similar results were found with waist circumference measurements. Measures of central rather than global adiposity (e.g., BMI) may be more predictive of prostate cancer, particularly for men of African descent because of different patterns of visceral fat deposition compared to those of European descent [Nemesure, 2014].

The HNF1β gene on 17q12 has been associated with both diabetes mellitus and prostate cancer. A meta-analysis of prostate cancer cases and controls showed that a particular allele, rs4420796, is associated with prostate cancer risk in both Caucasians and Asians, but not in African Americans. Investigation of this particular gene in African American samples is warranted. This, along with the high prevalence of diabetes in our study, is an incentive for genetic analysis of the blood samples that we have stored.

Further, there is recent and increasing evidence that the racial disparity that is seen in prostate cancer prevalence may be due in part to aberrant DNA methylation changes that switch off genes that suppress cell proliferation, apoptosis, and metastasis [Devaney et al., 2015]. In sum, this study

provides a resource for genetic analysis of African Americans with prostate cancer. We are looking to build on this work by genetic and/or epigenetic analyses of the samples.

Challenges

However, in the drive to recruit participants, an oversight error occurred in which there was a lapse in IRB approval and five participants were erroneously interviewed. Also, erroneously, a message was sent to the DOD that no participant recruitment took place. Based on communication with Creighton University partners indicating that there were 2 participants on their records interviewed between May 6th 2013 and July 22nd 2013, the JSU team instituted a review of activities and an additional three participants were discovered to have been interviewed outside the IRB approval coverage period. While the review was ongoing, the following actions were also taken:

1. JSU and Creighton University IRB were informed and JSU IRB requested for the report on activities review when ready.
2. All research staff underwent CITI training in responsible conduct of research
3. A letter was written to the DOD detailing the errors and the JSU co-PI spoke with the DOD IRB contact on the telephone to explain the discrepancy. The team was asked to send the report with the determination of the JSU IRB when ready.
4. Steps were taken to prevent any other occurrence in the future.
5. The five subjects were re-consented with a current IRB approved consent form.

IRB approval is in place and current at both study sites.

Another challenge was the departure of Dr. Ekundayo from JSU and the resulting process to change the Co-principal Investigator at Jackson State University. The impact was a slowing down of recruitment, interviews and blood collection.

Key Research Accomplishments

- Recruitment and training of study personnel: research project coordinators at both sites as well as two graduate students at Jackson State University.
- Development of a study specific Access database with embedded quality control measures that is used at both research sites.
- A collaborative meeting between the two research groups completed in year one and year two.
- Cultural proficiency training of all study personnel both at Creighton University and at Jackson State University.
- Subject recruitment measurements implemented through television, newspaper, community events, prostate cancer support groups, billboards and emails to community and church leaders, local urologists and all active physicians in the area.
- Identification of 662 eligible participants wherein 93 were interviewed at Creighton University and Jackson State University. Their data has been entered into the database and blood samples have been collected and stored on 44 participants who were eligible and volunteered to donate the sample.
- Prostate cancer prevention and health education occurred at each interview as well as during each television broadcast and community outreach project. Jackson State University also provided an educational presentation to a prostate cancer support group.
- Prostate cancer education was also provided to students in the masters of Public Health program as part of their curriculum.

Reportable Outcomes/Conclusion

My review, perhaps over the past 1 year, indicates that on the basis of accrued genetic interpretation, the bulk of these familial/hereditary inheritance patterns are consonant with an autosomal dominant mode of inheritance, although some rare autosomal recessive forms, such as in ataxia-telangiectasia,

may account for a limited number of prostate cancers. One theme that seems to be significant is that having a brother affected with PC has a stronger familial component than having a father with PC. This finding is surprising it seems to have been reported in some national, as well as international studies. In 2010, Whitman et al. and Hooker et al. identified at risk loci specific to prostate cancer in African Americans. These loci may be targets to test in the future on the stored DNA samples from participants in families with familial prostate cancer from this study.

During the recruitment process, we noted that a substantial proportion of the participants at the Omaha study site had originally lived in Southern states in the US, and in Mississippi, in particular. Thus, we expect that there is considerable overlap in both environmental exposures and genetic backgrounds among participants at the two sites.

During the course of the recruitment phase of the prostate cancer study funded by the DOD, we constantly attempted to accumulate data on African Americans (AAs) in North Omaha, their geographic area of most concentration in Nebraska. Information on prostate cancer predisposing genes in African Americans are partially reflected in the enclosed tables which are considered to be an important scientific area for continued study. Familial history may help us determine candidates for prostate-specific antigen (PSA) assessment. The involvement of our African American Co-PIs in both Omaha and Jackson have helped tremendously in our recruitment efforts and in the outreach to the AA community. Their efforts have been invaluable in terms of our ability to identify patients with PC in the community. However, a major concern throughout the study were the limitations involved in terms of identifying initial AA PC affected but their unwillingness, in most cases, to undergo a detailed family history assessment and, when indicated by us, to be of clinical-genetic importance with the need to follow-up with blood draws for ultimate molecular genetic investigation. We trained our staff on the value of cultural sensitivity, majority of our personnel look like the target community and we were very sensitive in our response to the questions asked by the participants. Unfortunately, some of the participants did not trust the system because of the vestiges of the Tuskegee Syphilis study that still lingers in their minds. Lack of trust, for whatever reason, resulted, we believe, in our inability to follow through with detailed family histories and ultimately lack of cooperation on the part of these AAs to allow blood draws for DNA collection and for ultimate molecular genetic involvement.

In addition, in Jackson, we faced difficulty in recruiting participants when the caller had an African, rather than a local African American, accent. This may be because it is common in Jackson for "cold calling" insurance sales people to be African and the typical response in the community is to hang up upon hearing the accent. Because of this experience, an African student's responsibilities were then changed from working with Dr. Ekundayo on outreach to working with Dr. Buxbaum detailing family structures. Sometimes spouses were suspicious of a female caller's reason for calling, even though packets of information had been sent including a letter from their trusted medical provider. In other cases, the reason for non-participation was not clear to the investigators, even after multiple follow-up calls. We noted that, once participants did agree to interview, it was common for participants' affects to change from guarded at the beginning to very open and talkative by the conclusion of the interview.

Between the two study sites we have identified 662 eligible participants for the study through local urologists, community recruitment and the immeasurable efforts of our staff. Ninety-three individuals have been interviewed with data entered and blood samples stored for the study. Multiple recruitment measures were implemented to increase recruitment numbers and raise interest in the communities.

Products

- An abstract on the study was accepted by the International Genetic Epidemiology Society (IGES) and a poster was presented at the IGES meeting in Baltimore in October, 2015 [Buxbaum, et al., 2015]. A manuscript is in preparation.

- An abstract was submitted to the APHA 2016 genomics forum:
  Prostate Cancer in African American Men
  Sarah Buxbaum, Carrie Snyder, Mark Stacey, Rasaki Aranmolate, Sade Kosoko-Lasaki, Ellastine Buckner, Olúgbémiga Ekúndayò and Henry Lynch.

Participants & Other Collaborating Organizations

Jackson State University, Jackson, Missouri
Sub-Contractor

Personnel reported on financial final report.

References

Woods VD, Montgomery SB, Herring RP. Recruiting Black/African American men for research on prostate cancer prevention. Cancer 2004;100(5):1017-25.

Ochs-Balcom HM, Rodriguez EM, Erwin DO. Establishing a community partnership to optimize recruitment of African American pedigrees for a genetic epidemiology study. J Community Genet 2011;2(4):223-31.

Shavers VL, Lynch CF, Burmeister LF. Factors that influence African-Americans' willingness to participate in medical research studies. Cancer 2001;91(1 Suppl):233-6.

Buxbaum SG, Snyder CL, Buckner E, Stacey ML, Aranmolate R, Kosoko-Lasaki O, Ekundayo OT, Lynch HT. Prostate Cancer in African American men. Presented at the International Genetic Epidemiology Society meeting on October 4-5, 2015.

Mandal DM, Sartor O, Halton SL, Mercante DE, Bailey-Wilson JE, Rayford W. Prostate Cancer Prostatic Dis. 2008 ; 11(3): 274–279. doi:10.1038/pcan.2008.5. Recruitment strategies and comparison of prostate cancerspecific clinical data on African-American and Caucasian males with and without family history.

Zeegers M.P., Jellema A., Ostrer H. Cancer. 2003. 97:1894–1903. Empiric risk of prostate carcinoma for relatives of patients with prostate carcinoma: A meta-analysis.
http://www.cdc.gov/diabetes/statistics/prev/national/fig2004.htm

Atchison EA, Gridley G, Carreon JD, Leitzmann MF, McGlynn KA. Int J Cancer. 2011. 128(3):635-43. doi: 10.1002/ijc.25362. Risk of cancer in a large cohort of U.S. veterans with diabetes.
Mitin T, Chen MH, Zhang Y, Moran BJ, Dosoretz DE, Katin MJ, Braccioforte MH, Salenius SA, D'Amico AV. J Urol. 2011. 186(6):2233-7. Diabetes mellitus, race and the odds of high grade prostate cancer in men treated with radiation therapy.

Park SY, Haiman CA, Cheng I, Park SL, Wilkens LR, Kolonel LN, Le Marchand L, Henderson BE. Cancer Causes Control. 2015. 26(10):1507-15. doi: 10.1007/s10552-015-0644-y. Racial/ethnic differences in lifestyle-related factors and prostate cancer risk: the Multiethnic Cohort Study.

Rhee H, Vela I, Chung E. Horm Cancer. 2015, in press. Metabolic syndrome and prostate cancer: a review of complex interplay amongst various endocrine factors in the pathophysiology and progression of prostate cancer.

Stopsack KH, Ziehr DR, Rider JR, Giovannucci EL. Cancer Causes Control. 2015, in press. Metformin and prostate cancer mortality: a meta-analysis.

Nemesure B, Wu S, Hennis A, Leske MC. Prostate Cancer in a Black Population (PCBP) Study Group. Cancer Epidemiol Biomarkers Prev. 2012. 21(5):851-8. doi: 10.1158/1055-9965.EPI-12-0071. Central adiposity and prostate cancer in a Black population.

Devaney JM, Wang S, Furbert-Harris P, Apprey V, Ittmann M, Wang B-D, Olender J, Lee NH, Kwabi-Addo B. Epigenetics. 2015. 10(4). doi: 10.1080/15592294.2015.1022019. Genome-wide differentially methylated genes in prostate cancer tissues from African-American and Caucasian men.

Whitman EJ, Pomerantz M, Chen Y, Chamberlin MM, Furusato B, Gao C, Ali A, Ravindranath L, Dobi A, Sestrehenn IA, McLeod DG, Srivastava S, Freedman M, Petrovics G. Prostate cancer risk allele specific for African descent associates with pathologic stage at prostatectomy. Cancer Epidmiol Biomarkers Prev 2010;19:1-8.

Hooker S, Hernandez W, Chen H, Robbins C, Torres JB, Ahaghotu C, Carpten J, Kittles RA. Replication of prostate cancer risk loci on 8q24, 11q13, 17q12, 19q33, and Xp11 in African Americans. Prostate 2010;70:270-275.

Appendices

Table 1: Recruitment Efforts

Successful

- Collaboration with local urologists in Omaha, Nebraska and Jackson, Mississippi
    - Utilization of medical students visiting directly with urologists was more successful than telephone contact
    - Majority of individuals recruited through this effort

Limited Success/Other Efforts

- Advertisement in Omaha Star, local newspaper dispersed in region of interest
- Advertisement by way of billboard in Omaha and Jackson
- Three appearances on local radio talk show, Real Talk and Health Matters
- Distributed information about the study at Black Health Family Fair two years in a row and attended one other local health fair in a local park
- Public Announcement released in local paper, Omaha World Herald
- Contacted leaders of the Neighborhood Associations in region of interest
- Reached out to church leaders who agreed to advertise the study in their church bulletins
- Multiple Barber Shop Blitz held in 2013 where local barbers spoke to clients about prostate cancer awareness and the study
- The Nebraska Tumor Registry mailed a letter to 380 African Americans with prostate cancer informing them of the study with informed consents, questionnaire and a postage paid envelope to indicate interest in the study.

Table 2: Participation and Recruitment by Site

Site	Identified	Recruited/Interviewed	Stored DNA
Creighton	125	26	7
Jackson State	537	67	37
Totals	662	93	44

Table 3. Multivariable regression with Age at Diagnosis as the outcome variable.

Variable	Coefficient	Standard error	T statistic	p-value
y-intercept	74.72	4.54	16.44	<0.001
Diabetes	3.24	1.66	1.95	0.0549
Embarrassment with Doctor	-2.83	0.99	-2.85	0.0055
Contaminated water	-6.16	2.99	-2.06	0.0425
Talk with Mother	-11.32	3.44	-3.29	0.0014

Figure 1: Study Interview Questionnaire

Date _____ **Interviewer:** _____ **JSU#**_____

Time Started: _____ **CU#** _____

SECTION 1: DEMOGRAPHICS and PERSONAL INFORMATION

D.1. Title ❒ Mr. ❒ Mrs. ❒ Ms. ❒ Miss ❒ Other_____

D.2. Name:_____
Last First Middle Maiden

_____
Street City State Zip

D.3 Home/Cell Phone: _____ **D.4. Work Phone:** _____

D.5. E-mail Address:_____

1.1 Birth Date:_____ **1.2** Part of a multiple birth? ❒ No ❒ Yes _____
(MMDDYYYY) (birth order)
❒ Twin ❒ Triplet

1.3. Gender: Female ❒ Male ❒

1.4. Marital Status: ❒ Never Married ❒ Single ❒ Widow(er) ❒ Married ❒ Divorced
❒ Separated ❒ Co-habiting

1.5. Race: Do you identify yourself as being African American?
❒ Yes ❒ No ❒ Multiple ❒ Decline to Answer
Please specify all racial groups you identify with by blood _____

1.6. Do you have: ❒ health care insurance? **1.7.** ❒ life insurance?
❒ private/group ❒ Medicare/Medicaid

1.7. Are you or other relatives adopted?
❒ No ❒ Yes → Name: _____ Relationship: _____
Name: _____ Relationship: _____

SECTION 2: MEDICAL HISTORY

2.1 a. Height in feet and inches_____ Current Weight in lbs _____
Wt. at age 18 _____ Wt. at age 30 _____ Wt. at age 40 _____
Heaviest Wt. _____ at age_____

b. Do you take aspirin or an aspirin substitute daily or every other day? ❒ No ❒ Yes
If yes, ❒ for pain? ❒ for heart/stroke prevention? ❒ Other: _____
How long? _____
(years and months)

2.2 Cancer History

a. Have you ever been diagnosed with cancer?
❒ No ❒ Yes → Please list date(s) of diagnosis, original site(s)/type(s) of cancer (such as colon cancer, leukemia, breast cancer), and how the cancer was detected.

Date	Site	How detected	
		during check-up	due to symptoms; type of symptoms (please write)

b. Have you or one of your relatives been diagnosed with a **hereditary disorder**?
❒ No ❒ Yes → please specify _____

2.3 Prostate Cancer History

Have you had any of the following screenings:

a. **digital rectal exam**? ❒ No ❒ Yes → age of first? _____
on a regular basis? ❒ No ❒ Yes → How often?_____
b. **blood test for prostate cancer** (PSA-prostate specific antigen)?
❒ No ❒ Yes → age of first? _____
on a regular basis? ❒ No ❒ Yes → How often?_____

Have you ever had:

a. **an enlarged prostate**? ❒ No ❒ Yes; Date: _____
if yes, did you have surgery? ❒ No ❒ Yes Date: _____
b. **a positive PSA level**? ❒ No ❒ Yes; Date: _____

2.4 Other Medical Conditions

Have you been diagnosed with any of the following conditions? (Please select all that apply)

❒ anemia (chronic)
❒ diabetes
❒ hypertension (high blood pressure)
❒ sleep problems
❒ heartburn (GERD)
❒ glaucoma
❒ Crohn's disease
❒ ulcerative colitis
❒ obesity
❒ alcoholism
❒ psychiatric problem
❒ Other: _____

2.5 Physical Activity

a.

	None	Very light	Light	Moderate	Somewhat hard	Hard	Very hard
Childhood	❒	❒	❒	❒	❒	❒	❒
High school	❒	❒	❒	❒	❒	❒	❒
19-29	❒	❒	❒	❒	❒	❒	❒
30-39	❒	❒	❒	❒	❒	❒	❒
40-49	❒	❒	❒	❒	❒	❒	❒
50-59	❒	❒	❒	❒	❒	❒	❒
60-69	❒	❒	❒	❒	❒	❒	❒
70-79	❒	❒	❒	❒	❒	❒	❒

b. Currently how frequently do you exercise? _____

c. How much of your work involves physical activity?
❒ None ❒ A little ❒ Some ❒ Most ❒ Nearly all ❒ All

d. How much of your daily routine involves physical activity?
❒ None ❒ A little ❒ Some ❒ Most ❒ Nearly all ❒ All

SECTION 3: SOCIAL HISTORY

3.1: Highest level of education ❒ Elementary School ❒ Middle School ❒ High School ❒ GED ❒ Technical/Vocational Certificate Degree ❒ College/Postgraduate

3.2: Income and Employment:

a. **Income during:**	**Childhood**	**Now**
None	❒	❒
Up to 4,999	❒	❒
5,000-14,999	❒	❒
15,000-29,999	❒	❒
30,000-49,000	❒	❒
50,000-59,000	❒	❒
60,000-69,000	❒	❒
70,000-79,000	❒	❒
80,000 and above	❒	❒

b. **Current Employment Status**
❒ Full time
❒ Part time
❒ Unemployed
❒ Retired
❒ Self-employed

c. **Employment History**

Date Range	Type of work or title	# of years	Exposure to any of the following? (check all that apply) Asbestos	Paints/Solvents	Benzene	Engine exhaust	Lead
			❒	❒	❒	❒	❒
			❒	❒	❒	❒	❒
			❒	❒	❒	❒	❒
			❒	❒	❒	❒	❒
			❒	❒	❒	❒	❒
			❒	❒	❒	❒	❒

d. Do you receive government assistance? ❒ Yes ❒ No ❒ Decline to answer

e. Total hours worked each day: _____

3.3. Housing Type:

a. ❒ Homeowner ❒ Rent b. ❒ Home ❒Apartment ❒ Condominium❒ Mobile Home

c. I live: ❒ alone ❒ with family ❒ with friends d. How many people live in your household? _____

3.4. Neighborhood:

a. I feel that my neighborhood is safe. ❒ Yes ❒ No
b. I know where the parks are in my neighborhood. ❒ Yes ❒ No
c. I use the parks in my neighborhood. ❒ Yes ❒ No
d. I know the recreational organizations in my neighborhood. ❒ Yes ❒ No
e. My neighborhood has places where I can walk. ❒ Yes ❒ No
f. I walk or run there ❒ Daily ❒ 4 Times/week ❒ Twice/week ❒ Weekly
❒ Twice a month ❒ Less than twice a month ❒ Never

3.5. Please rate how much you agree with the following statements regarding your neighborhood?
1= Strongly Agree 2= Agree 3= Neutral 4= Disagree 5= Strongly Disagree

a. Most people in my neighborhood can be trusted. _____
b. In my neighborhood you have to be alert or someone is likely to take advantage of you. _____
c. Most people in my neighborhood are willing to help if needed. _____
d. In my neighborhood people generally do not trust each other in matters of lending or borrowing money. _____

3.6. Transportation:

a. I have a vehicle. ❒ Yes ❒ No
b. If no, I travel by: ❒ taxi ❒ bus ❒ friend/neighbor ❒ family member
c. I have to travel _____ miles to buy food.
d. I have to travel _____ miles to see my doctor.
e. When I go out I mostly go with: (check only one)
❒ Family ❒ Friends ❒ Neighbors ❒ Co-workers ❒ Self ❒ Other _____

SECTION 4: PSYCHOSOCIAL HISTORY

4.1. Childhood:

a. I grew up in the same household with: (Please check all that apply.)

❒ My mother ❒ Grandparent(s) ❒ Cousin(s) ❒ Sibling(s)
❒ My father ❒ Aunt/Uncle ❒ Adopted ❒ Other; _____

b. As a child I lived in: ❒ a big city ❒ a small city ❒ a small town ❒ a suburb ❒ a rural area ❒ a farm

c. For Mississippi Participants:

As a child I lived in: ❒ The Delta area ❒ Northeast MS ❒ Central MS
❒ Southern MS ❒ Coastal MS ❒ Southwest
❒ Other:_____

d. For Nebraska Participants:

As a child I lived in: ❒ North Omaha ❒ South Omaha ❒ Midtown
❒ West Omaha ❒ Other: _____

e. Please indicate the places you have lived (all participants)

Dates or Ages	Place (City, State)	# of Years	Exposure to any of the following? (check all that apply) Asbestos	Paints/Solvents	Benzene	Engine exhaust	Lead	Contaminated Water
			❒	❒	❒	❒	❒	❒
			❒	❒	❒	❒	❒	❒
			❒	❒	❒	❒	❒	❒
			❒	❒	❒	❒	❒	❒
			❒	❒	❒	❒	❒	❒
			❒	❒	❒	❒	❒	❒

f. As a child we attended religious services: ❒ regularly ❒ occasionally ❒ on holidays ❒ never

4.2. Communication, Trust and Attitudes towards Self

a. Do you have anyone you discuss your health concerns with? ❒ No ❒ Yes

b. If yes, please indicate who. (Please check as many as apply.)

❒ Father ❒ Sibling(s) ❒ Friend ❒ Doctor
❒ Mother ❒ Children ❒ Cousin ❒ Counselor
❒ Wife ❒ Uncle ❒ Co-Worker ❒ Other, _____
❒ Husband ❒ Aunt ❒ Pastor

b. To what extent do you trust the following groups of people?

	Extremely	Quite a bit	Moderately	A little bit	None
i. People from your race/ethnic group	❒	❒	❒	❒	❒
ii. People from other race/ethnic groups	❒	❒	❒	❒	❒
iii. Local government officials	❒	❒	❒	❒	❒
iv. State government officials	❒	❒	❒	❒	❒
v. Federal government officials	❒	❒	❒	❒	❒
vi. Police	❒	❒	❒	❒	❒
vii. Your health care provider	❒	❒	❒	❒	❒

c. How much do you agree with the following statements with regard to your attitudes towards yourself?

1= Strongly Agree 2= Agree 3= Neutral 4= Disagree 5= Strongly Disagree

i. I am embarrassed to go see the doctor. _____
ii. I feel I am treated with care and respect by my health care provider(s) _____

d. How often do you feel the following:

	Always	Often	Rarely	Never
i. stressed	❒	❒	❒	❒
ii. misunderstood	❒	❒	❒	❒
iii. not listened to	❒	❒	❒	❒

SECTION 5: ENVIRONMENTAL HISTORY

5.1. Environmental

a. Have you used any form of tobacco regularly?

❒ No

❒ Yes → what type(s)? ❒ cigarettes → number of packs per day? _____
❒ pipe
❒ cigars
❒ chewing tobacco
❒ snuff

b. at what age did you start? _____
c. at what age did you stop? _____
d. total numbers of years smoked? _____
e. lived in the same house with a smoker (if a nonsmoker)? ❒ No
❒ Yes → # of years? _____

5.2. a. Have you ever consumed alcoholic drinks?

❒ No

❒ Yes → how many per week? ❒ 0-3 ❒ 4-9 ❒ 10+

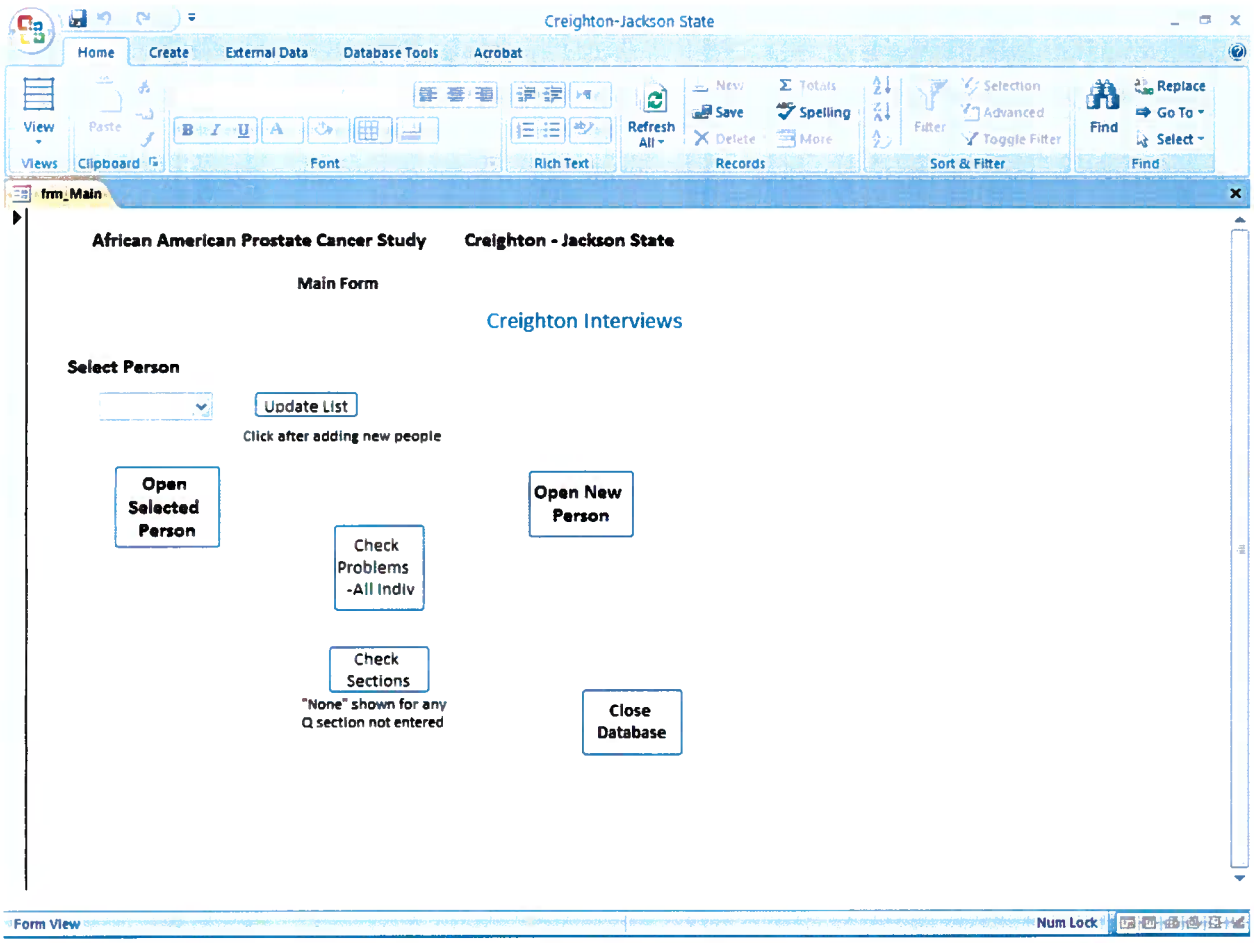
what type(s)? _____

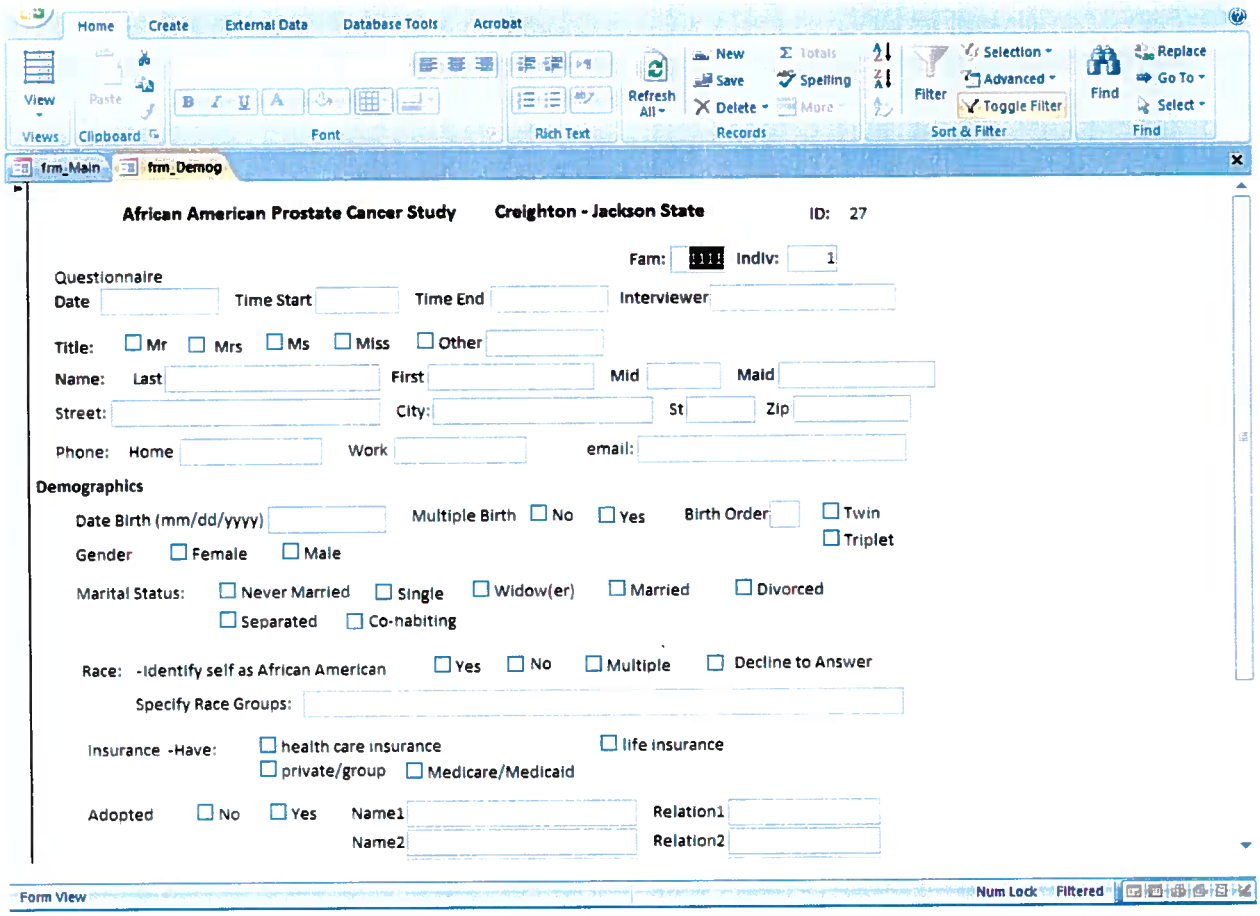
b. at what age did you start? _____
c. at what age did you stop? _____
d. total numbers of years? _____

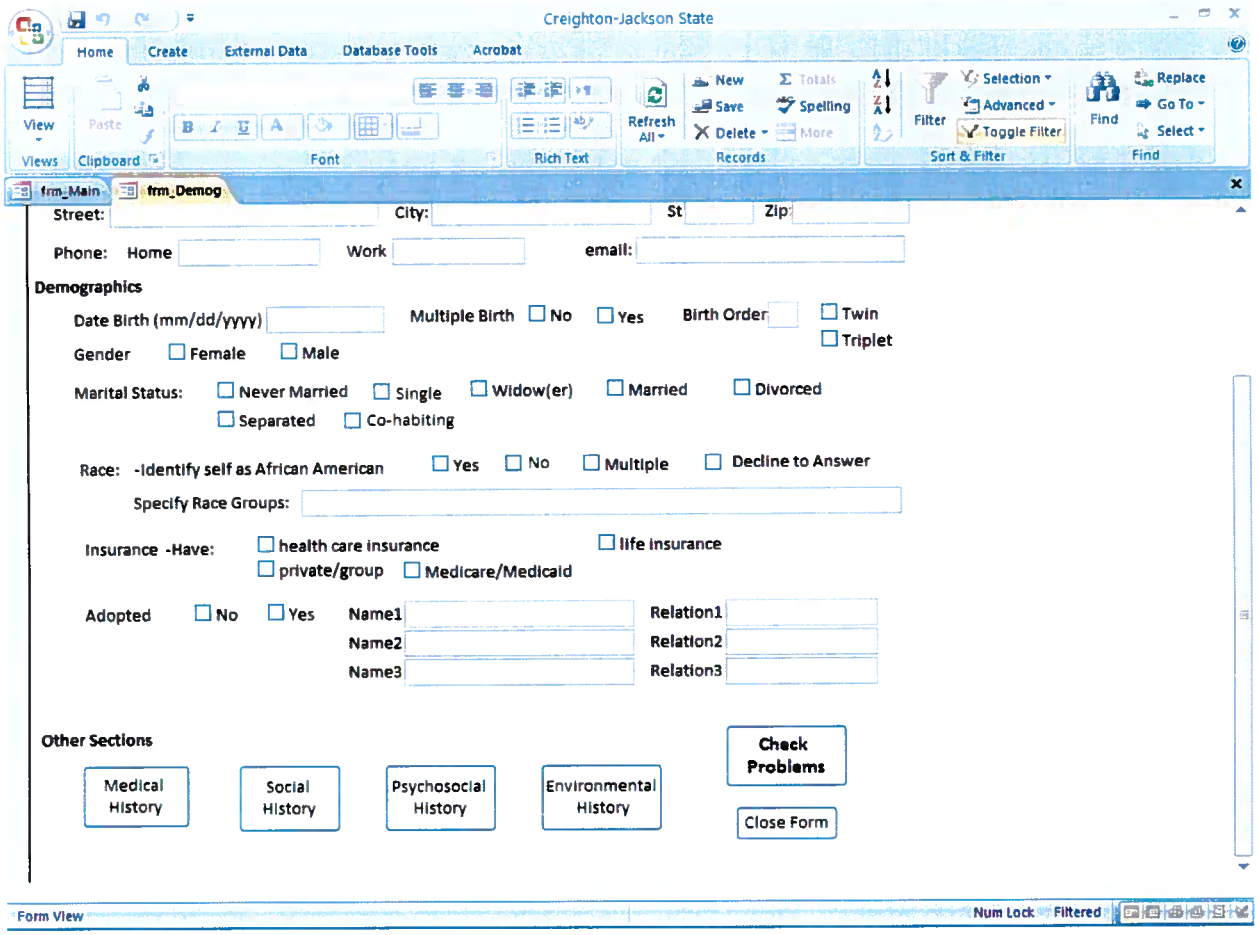
THANK YOU FOR YOUR TIME AND CONTRIBUTION!

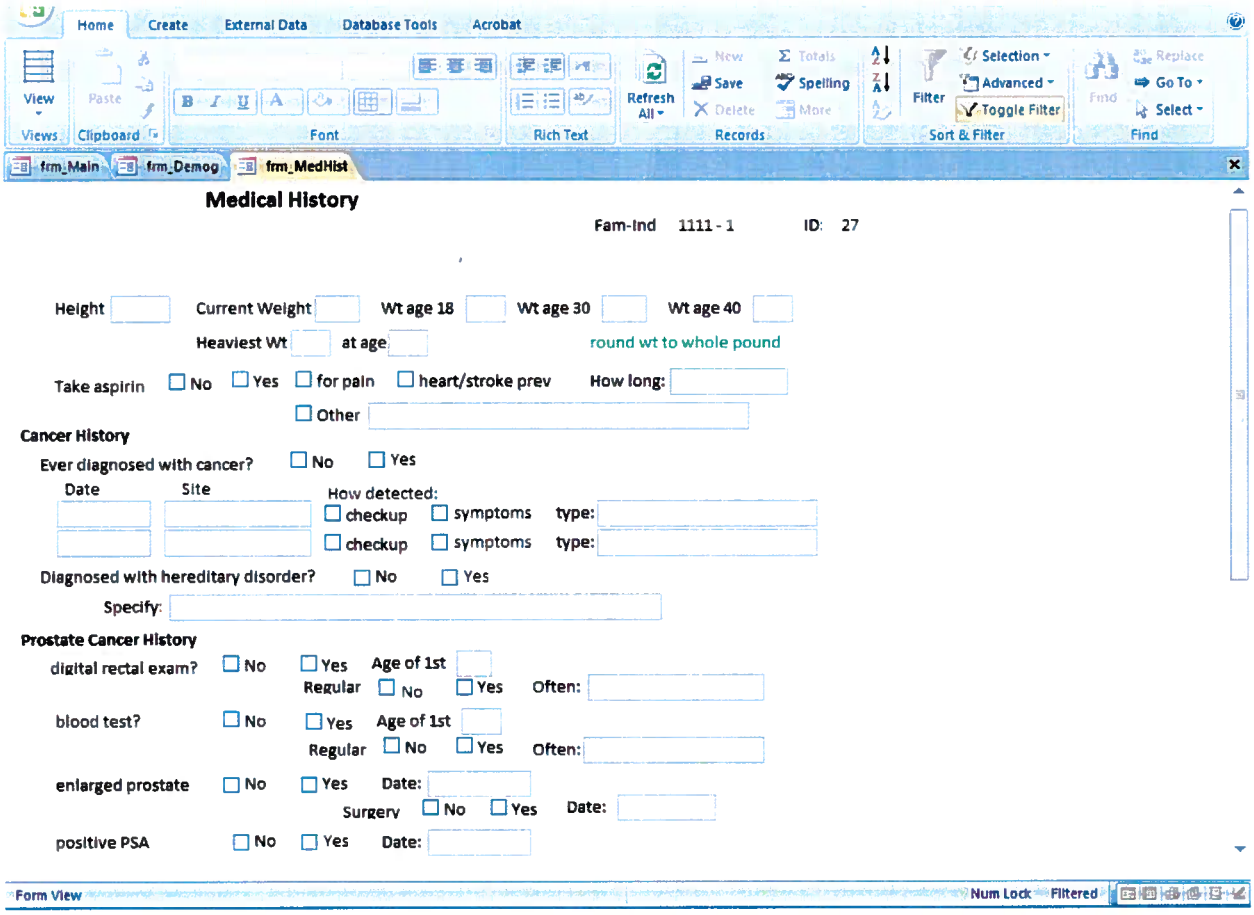
Time Ended: _____ Interviewer Initials: _____

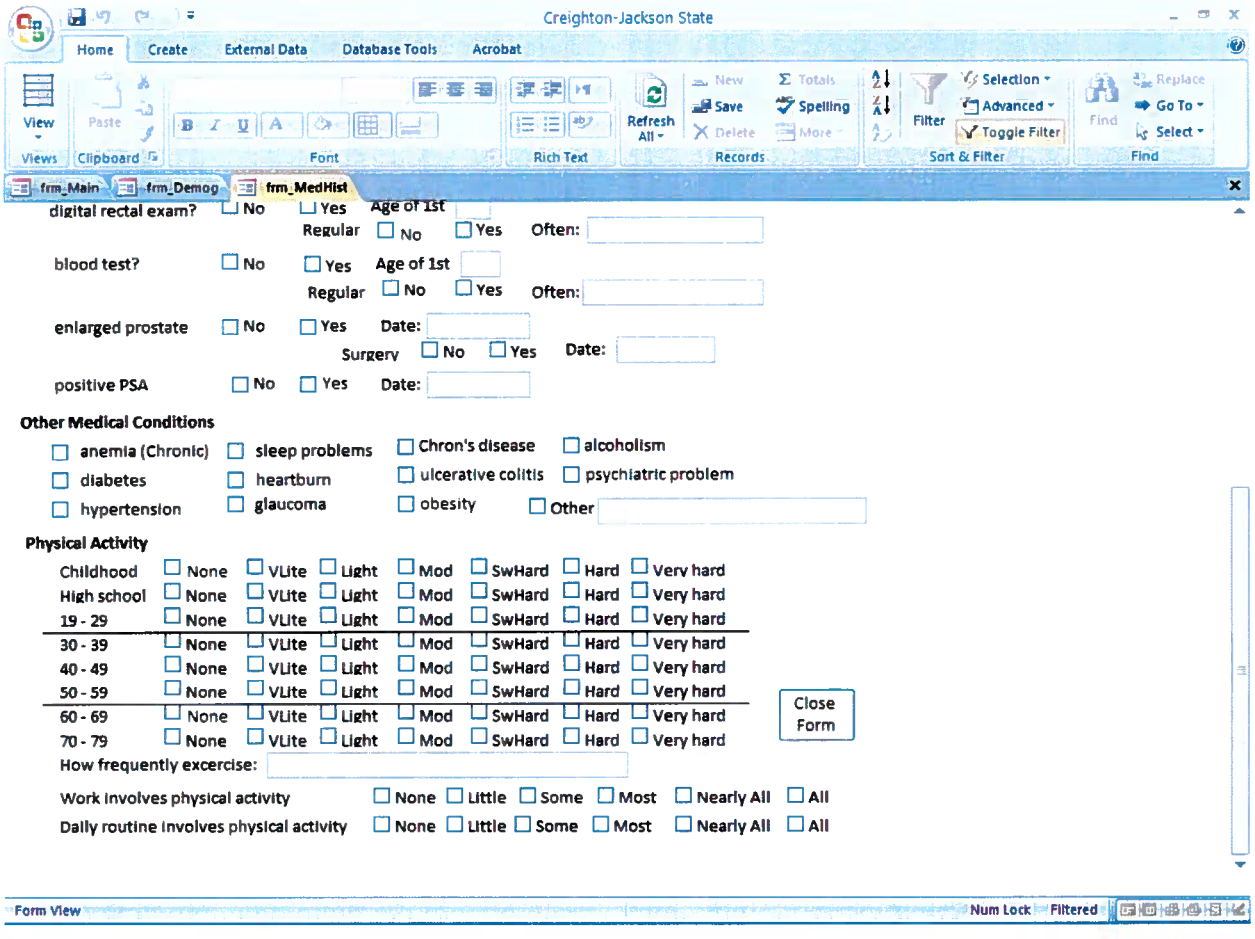
Figure 2: Prostate Cancer in African Americans Database and Notes

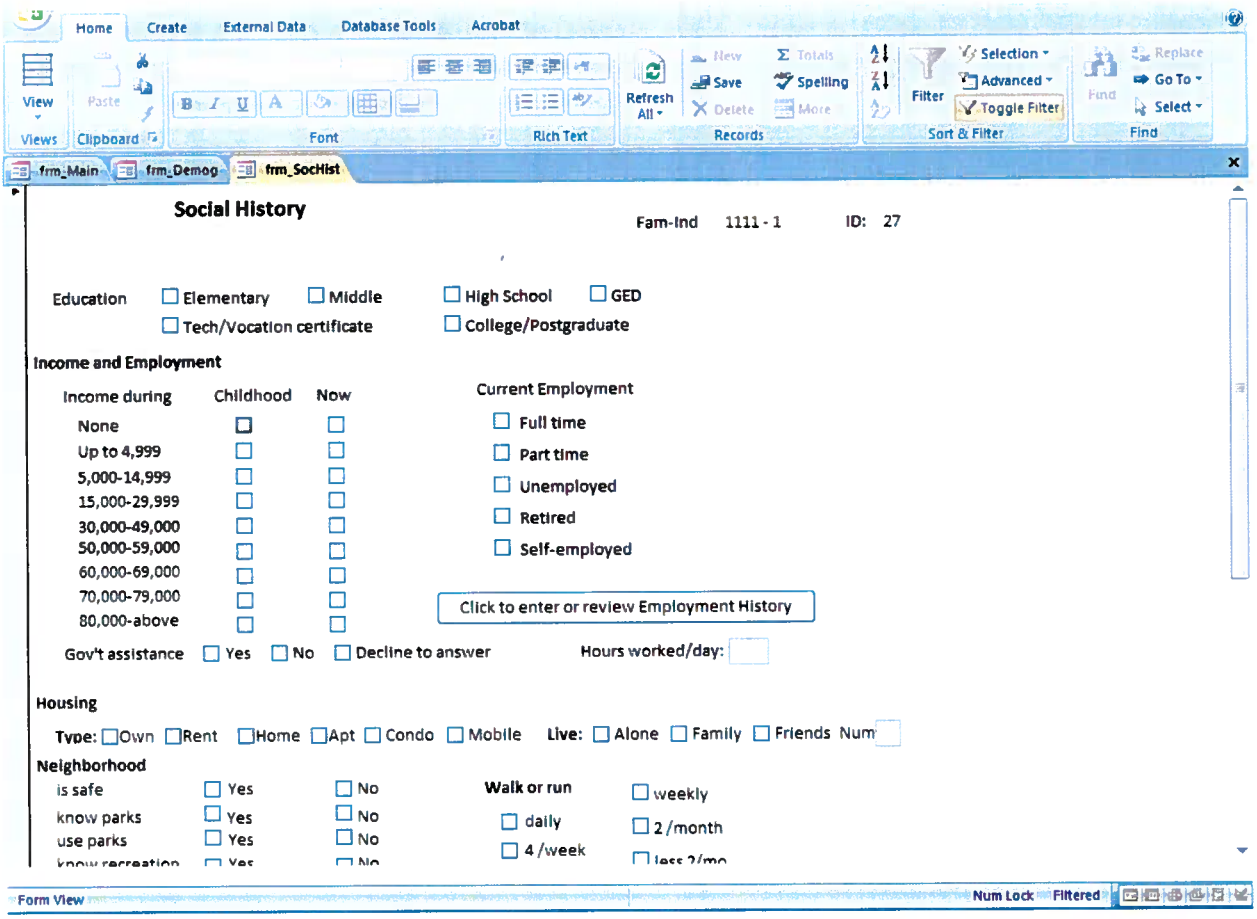

Creighton-Jackson State
Home
Create
External Data
Database Tools
Acrobat
frm_Main
African American Prostate Cancer Study
Creighton - Jackson State
Main Form
Creighton Interviews
Select Person
Update List
Click after adding new people
Open Selected Person
Open New Person
Check Problems -All Indiv
Check Sections
"None" shown for any Q section not entered
Close Database
Form View
Num Lock

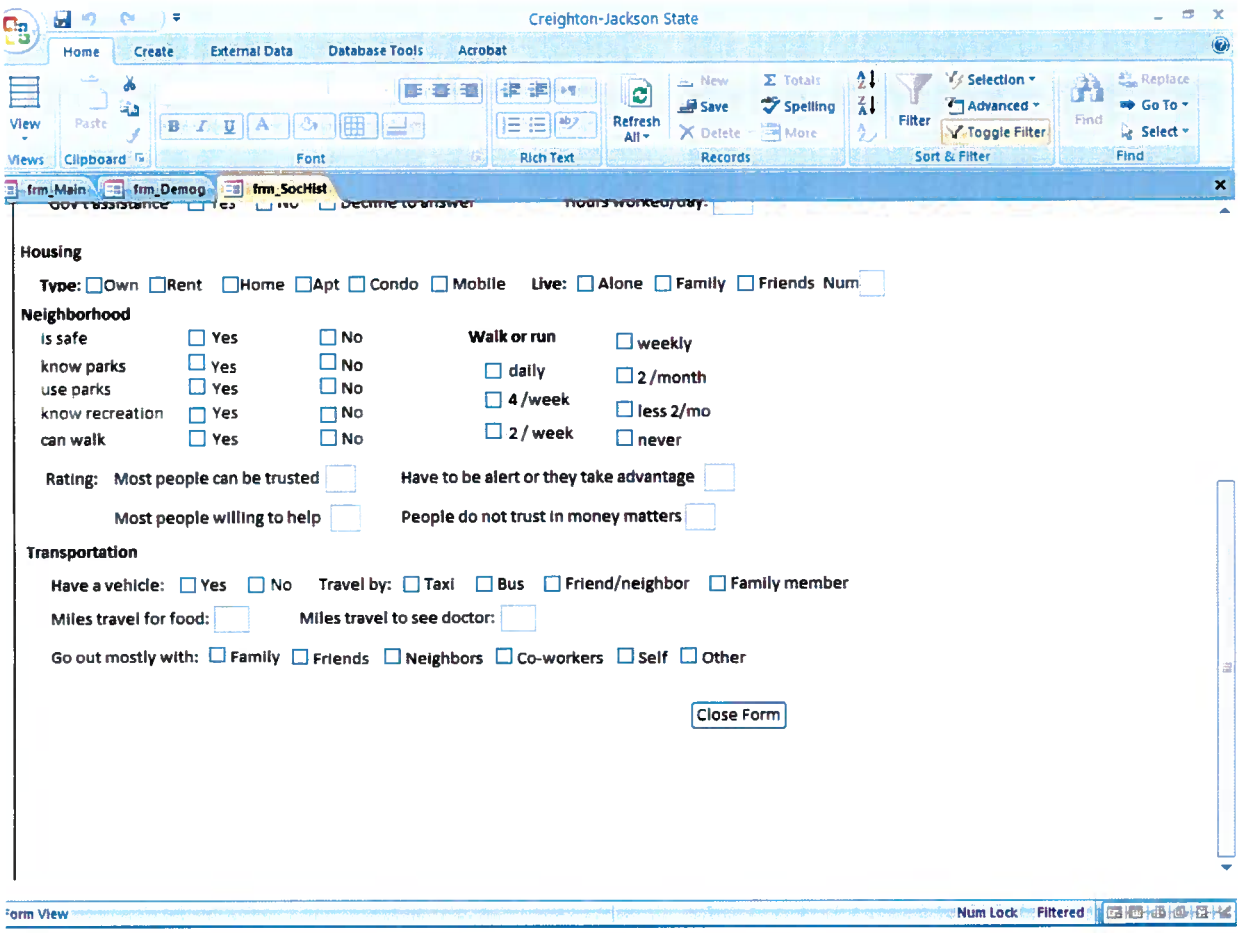

Home
Create
External Data
Database Tools
Acrobat
frm_Main
frm_Demog
African American Prostate Cancer Study
Creighton - Jackson State
ID: 27
Fam:
Indiv: 1
Questionnaire
Date
Time Start
Time End
Interviewer
Title: Mr Mrs Ms Miss Other
Name: Last First Mid Maid
Street:
City:
St
Zip
Phone: Home
Work
email:
Demographics
Date Birth (mm/dd/yyyy)
Multiple Birth No Yes
Birth Order
Twin
Triplet
Gender Female Male
Marital Status: Never Married Single Widow(er) Married Divorced
Separated Co-habiting
Race: -Identify self as African American Yes No Multiple Decline to Answer
Specify Race Groups:
Insurance -Have: health care insurance life insurance
private/group Medicare/Medicaid
Adopted No Yes
Name1
Relation1
Name2
Relation2
Form View
Num Lock
Filtered

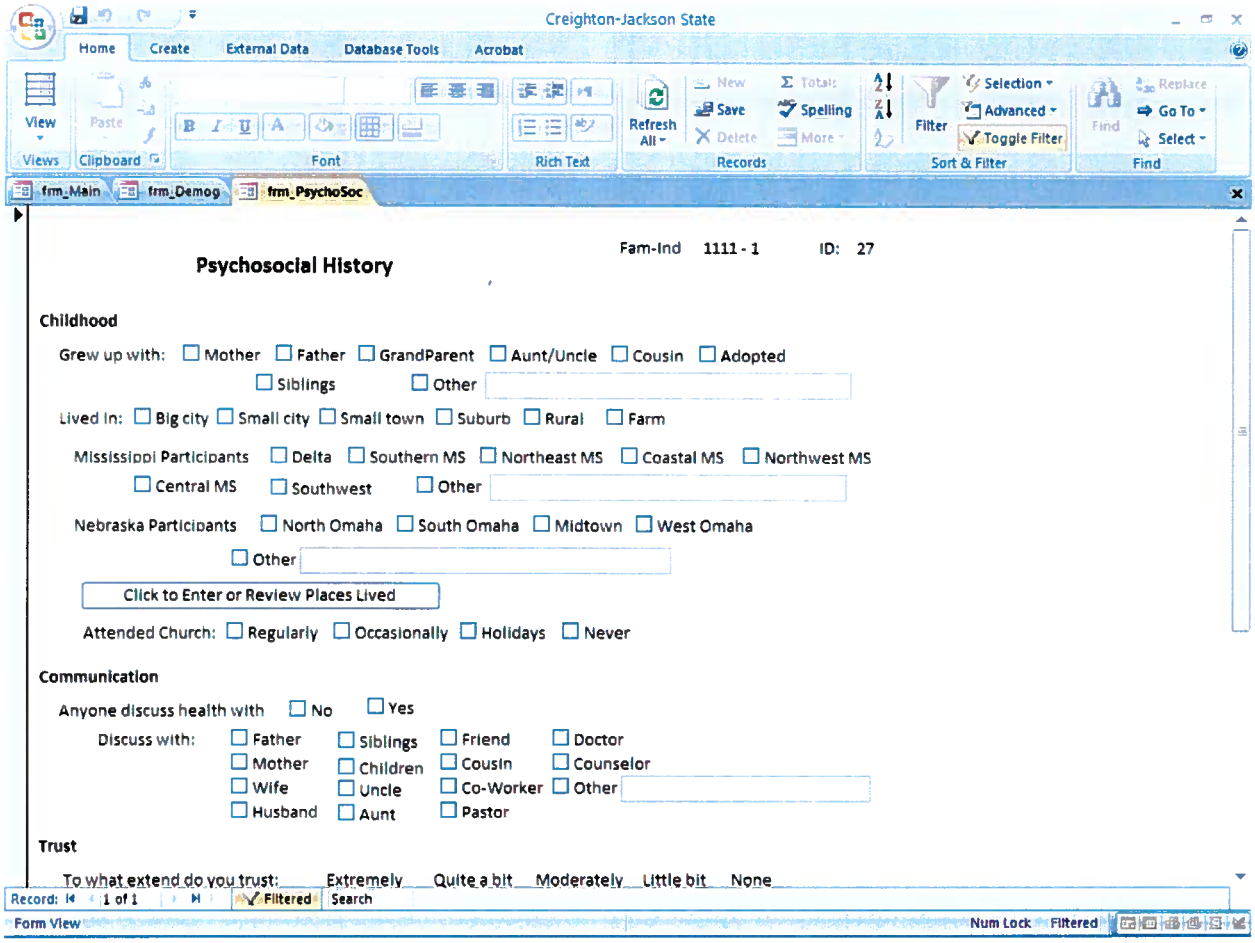

Creighton-Jackson State
Home
Create
External Data
Database Tools
Acrobat
frm_Main
frm_Demog
Street:
City:
St
Zip
Phone: Home
Work
email:
Demographics
Date Birth (mm/dd/yyyy)
Multiple Birth No Yes
Birth Order
Twin
Triplet
Gender Female Male
Marital Status: Never Married Single Widow(er) Married Divorced
Separated Co-habiting
Race: -Identify self as African American Yes No Multiple Decline to Answer
Specify Race Groups:
Insurance -Have: health care insurance life insurance
private/group Medicare/Medicaid
Adopted No Yes
Name1
Relation1
Name2
Relation2
Name3
Relation3
Other Sections
Medical History
Social History
Psychosocial History
Environmental History
Check Problems
Close Form
Form View
Num Lock
Filtered

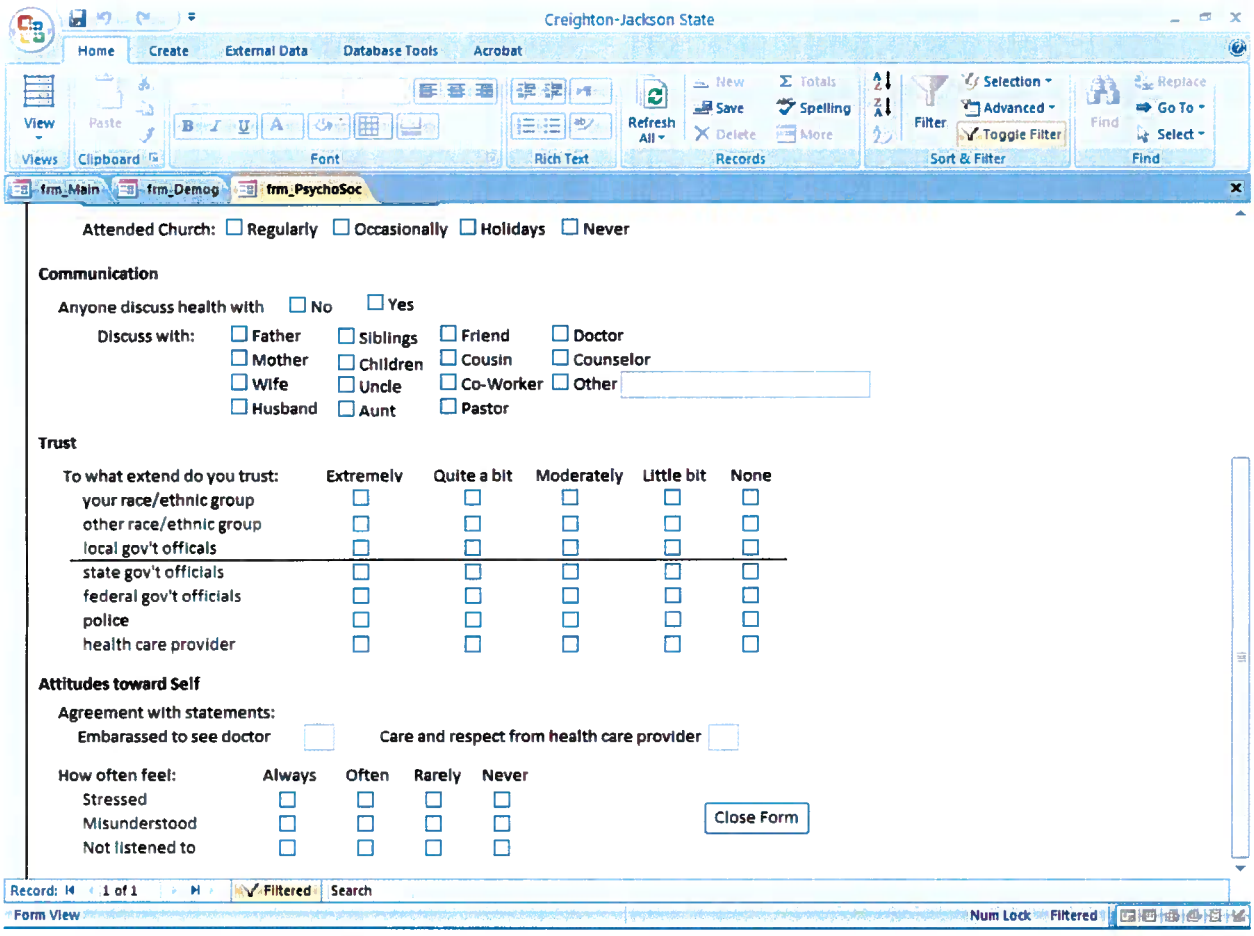

Home
Create
External Data
Database Tools
Acrobat
frm_Main
frm_Demog
frm_MedHist
Medical History
Fam-Ind 1111 - 1
ID: 27
Height
Current Weight
Wt age 18
Wt age 30
Wt age 40
Heaviest Wt
at age
round wt to whole pound
Take aspirin
No
Yes
for pain
heart/stroke prev
How long:
Other
Cancer History
Ever diagnosed with cancer?
No
Yes
Date
Site
How detected:
checkup
symptoms
type:
Diagnosed with hereditary disorder?
Specify:
Prostate Cancer History
digital rectal exam?
Age of 1st
Regular
Often:
blood test?
enlarged prostate
Date:
Surgery
positive PSA
Form View
Num Lock
Filtered

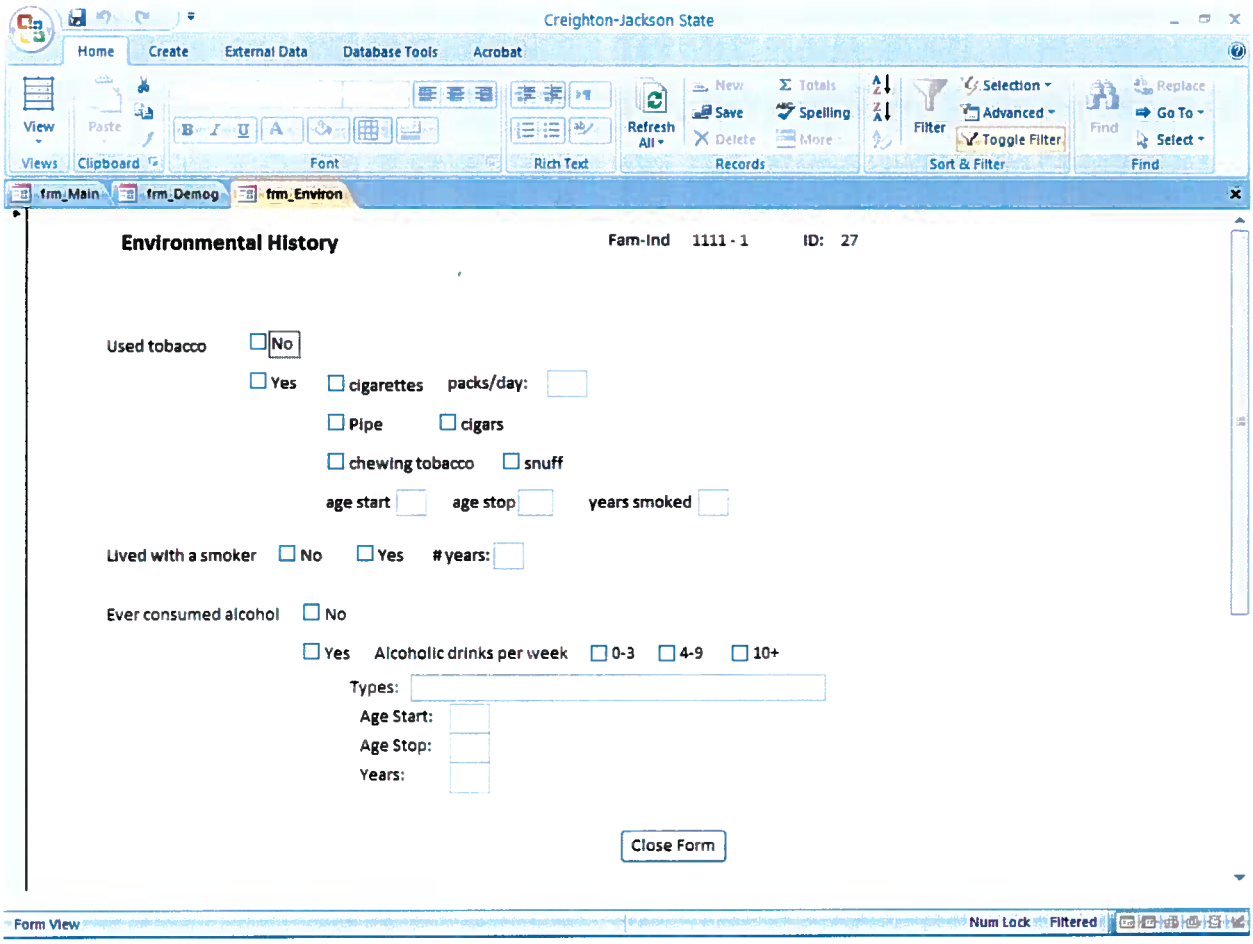

Creighton-Jackson State
Home
Create
External Data
Database Tools
Acrobat
frm_Main
frm_Demog
frm_MedHist
digital rectal exam?
Age of 1st
Regular
Often:
blood test?
enlarged prostate
Date:
Surgery
positive PSA
Other Medical Conditions
anemia (Chronic)
sleep problems
Chron's disease
alcoholism
diabetes
heartburn
ulcerative colitis
psychiatric problem
hypertension
glaucoma
obesity
Other
Physical Activity
Childhood
High school
19 - 29
30 - 39
40 - 49
50 - 59
60 - 69
70 - 79
None
VLite
Light
Mod
SwHard
Hard
Very hard
Close Form
How frequently excercise:
Work involves physical activity
Daily routine involves physical activity
Little
Some
Most
Nearly All
All
Form View
Num Lock
Filtered


Home
Create
External Data
Database Tools
Acrobat
frm_Main
frm_Demog
frm_SocHist
Social History
Fam-Ind 1111 - 1
ID: 27
Education
Elementary
Middle
High School
GED
Tech/Vocation certificate
College/Postgraduate
Income and Employment
Income during
Childhood
Now
None
Up to 4,999
5,000-14,999
15,000-29,999
30,000-49,000
50,000-59,000
60,000-69,000
70,000-79,000
80,000-above
Current Employment
Full time
Part time
Unemployed
Retired
Self-employed
Click to enter or review Employment History
Gov't assistance
Yes
No
Decline to answer
Hours worked/day:
Housing
Type: Own Rent Home Apt Condo Mobile
Live: Alone Family Friends Num
Neighborhood
is safe
know parks
use parks
Yes
No
Walk or run
daily
4 /week
weekly
2 /month
Form View
Num Lock
Filtered


Creighton-Jackson State
Home
Create
External Data
Database Tools
Acrobat
frm_Main
frm_Demog
frm_SocHist
Housing
Type: Own Rent Home Apt Condo Mobile
Live: Alone Family Friends Num
Neighborhood
is safe
know parks
use parks
know recreation
can walk
Yes
No
Walk or run
daily
4 /week
2 / week
weekly
2 /month
less 2/mo
never
Rating:
Most people can be trusted
Have to be alert or they take advantage
Most people willing to help
People do not trust in money matters
Transportation
Have a vehicle: Yes No
Travel by: Taxi Bus Friend/neighbor Family member
Miles travel for food:
Miles travel to see doctor:
Go out mostly with: Family Friends Neighbors Co-workers Self Other
Close Form
Form View
Num Lock
Filtered


Creighton-Jackson State
Home
Create
External Data
Database Tools
Acrobat
frm_Main
frm_Demog
frm_PsychoSoc
Fam-Ind 1111 - 1 ID: 27
Psychosocial History
Childhood
Grew up with: Mother Father GrandParent Aunt/Uncle Cousin Adopted
Siblings Other
Lived in: Big city Small city Small town Suburb Rural Farm
Mississippi Participants Delta Southern MS Northeast MS Coastal MS Northwest MS
Central MS Southwest Other
Nebraska Participants North Omaha South Omaha Midtown West Omaha
Other
Click to Enter or Review Places Lived
Attended Church: Regularly Occasionally Holidays Never
Communication
Anyone discuss health with No Yes
Discuss with: Father Siblings Friend Doctor
Mother Children Cousin Counselor
Wife Uncle Co-Worker Other
Husband Aunt Pastor
Trust
To what extend do you trust: Extremely Quite a bit Moderately Little bit None
Record: 1 of 1
Filtered
Search
Form View
Num Lock
Filtered


Creighton-Jackson State
frm_Main
frm_Demog
frm_PsychoSoc
Attended Church: Regularly Occasionally Holidays Never
Communication
Anyone discuss health with No Yes
Discuss with: Father Siblings Friend Doctor
Mother Children Cousin Counselor
Wife Uncle Co-Worker Other
Husband Aunt Pastor
Trust
To what extend do you trust: Extremely Quite a bit Moderately Little bit None
your race/ethnic group
other race/ethnic group
local gov't officals
state gov't officials
federal gov't officials
police
health care provider
Attitudes toward Self
Agreement with statements:
Embarassed to see doctor
Care and respect from health care provider
How often feel: Always Often Rarely Never
Stressed
Misunderstood
Not listened to
Close Form
Record: 1 of 1
Filtered
Search
Form View
Num Lock
Filtered


Creighton-Jackson State
Home
Create
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Database Tools
Acrobat
frm_Main
frm_Demog
frm_Environ
Environmental History
Fam-Ind 1111 - 1
ID: 27
Used tobacco
No
Yes
cigarettes
packs/day:
Pipe
cigars
chewing tobacco
snuff
age start
age stop
years smoked
Lived with a smoker
No
Yes
years:
Ever consumed alcohol
No
Yes
Alcoholic drinks per week
0-3
4-9
10+
Types:
Age Start:
Age Stop:
Years:
Close Form
Form View
Num Lock
Filtered

African American Prostate Cancer Study
Creighton - Jackson State
Questionnaire Database Notes

Overview

Two identical Microsoft Access databases are used to record questionnaire responses. One, located in Omaha and named Prostate_CU, is used for Creighton managed interviews. The other, located in Jackson and named Prostate_JSU, is used for Jackson State managed interviews. They are designed to run with the 2007 version of MS Access.

Each database has a main screen plus a screen for each section of the questionnaire. The section screens (Demographics, Medical, Social, etc.) roughly mimic the layout of the questionnaire. Each input item has a label that is abbreviated from the question. Two items, employment history and places lived, have a button that opens a screen where multiple responses can be listed. The demographics screen also serves as a control for the person since it contains buttons that open each of the other screens for that individual. The database contains edit checks on the input data. There are buttons that list problems, and message boxes that alert to a probable error.

Each person is identified in the database with a Family – Individual number (Fam-Indiv). When a person is first input, the database assigns an ID number to the person that is used by the database to coordinate the records for that person. Although the ID is shown on the screens, it can be ignored by someone doing data input. It is assumed there will be only one questionnaire in the database for each individual.

Data Input and Navigation

When the database is opened, the Main Form automatically appears. This form is used for control purposes. There are 2 ways to open the data for a person.

1) Use the Open Selected Person button. This goes directly to the data for the individual highlighted in the Select Person drop down box at the upper left of the screen. Click on the down arrow to see a list of Fam-Indiv numbers, then click on the desired person. After selecting the person, click the Open Selected Person button to go to the Demographics screen. To have a complete list in the drop down box, there is an Update List button that must be clicked after new individuals have been added. This method is used to return to a previously entered person for edit or review.
2) Use the Open New Person button. This will open a blank Demographics screen. Start by entering the Fam-Indiv numbers, then proceed with the remainder of the data.

The Demographics screen contains the personal and demographic inputs for the individual. It also contains buttons to open the four history sections of the questionnaire. Always use these buttons to open the history forms.

Always close each history form before going to another form. This is important because forms left open can cause data to be linked to the wrong person! Use the Close Form button on each form, because some include edit checks. When a history form is closed, the process returns to the Demographics form, and another history form can be selected.

The Social History form has a button to open the Employment History form. The Psychosocial History form has a button to open the Places Lived form. Multiple items can be entered on these forms. Always close these forms, and use the Close Form button to do so.

Much of the input is to check boxes. Use the mouse to check the box corresponding to the answer checked on the questionnaire. Some of the forms have date inputs, and a small calendar appears to the right when the input is selected. The format is mm/dd/yyyy, and it may be easier to type the date than to scroll the calendar. Exceptions are the employment history and places lived, which are free-form entry text boxes. The tab order on the forms often skips the check boxes. When using the tab key, it is possible to tab past the current form which opens a new form. This should be avoided, and a red warning to close the form will appear below the Close Form button.

The Demographics screen also has a Check Problems button which runs a query listing any input problems found for the person. The query is closed by clicking the x to the right of the qProblems tab. Use the Close Form button on the Demographics form to return to the main form.

The Main Form has a Check Problems –All Indiv button which runs a query listing input problems found by the edit checks for all persons in the database. More on these edits in the Edit Checks section below. The query is closed by clicking the x to the right of the qProblems tab. The Check Sections button runs a query that reports, for any person entered in the Demographics section, any history sections which have no data entered. In this case "None" will appear under the section name. The query is closed by clicking the x to the right of the qCheckSections tab. The form also has a Close Database button, used to exit the database.

Edit Checks

Many of the questions have edit checks. These cause message boxes to appear stating the problem. Clicking OK closes the message, but the input person needs to fix the problem or it will remain in the saved data. A common check is conflicting answers, e.g. both Yes and No, Male and Female, Twin and Triplet, Light and Hard, None and All. Checks where only one should be selected are included, e.g. Title, Marital Status, Income level, Housing Type. Ratings must be 1 through 5. Questions with additional information if Yes may show a message if No is checked and the Yes information is entered. If the weight at any age is more than Heaviest Wt, a message will appear.

These edits also appear on the lists from the Check Problems buttons if not resolved before the button is clicked. Additional checks on the lists are for questions that are not answered. The lists can be printed for follow-up.

Database Structure

Each form (except frm_Main) has a table to hold data for that form. The demographics table (tbl_Demogr) has field "ID" which is an autonumber, meaning the database automatically creates the ID when data is first entered for a person on the demographics form. All other tables contain the ID field, which is the link to the person's identity in the demographics table (including the Fam-Indiv number). Each table has its' own sysid field,

which is an autonumber that provides a unique identifier for that record. Table ErrorList is a temporary table for holding the results from the Check Problems buttons, driven by VBA code in module ErrorFind. Each form has VBA code for navigation and error checking purposes, often using Click and AfterUpdate methods.

Figure 3: Prostate Cancer Education Program

- **Definition**

  Cancer that forms in tissues of the prostate (a gland in the male reproductive system found below the bladder and in front of the rectum). Prostate cancer usually occurs in older men.

- **Risk factors for Prostate Cancer**
  - **Age over 65**: Age is the main risk factor for prostate cancer. The chance of getting prostate cancer increases as you get older. In the United States, most men with prostate cancer are over 65. This disease is rare in men under 45.
  - **Family history**: Your risk is higher if your father, brother, or son had prostate cancer.
  - **Race**: Prostate cancer is more common among black men than white or Hispanic/Latino men. It's less common among Asian/Pacific Islander and American Indian/Alaska Native men.
  - **Certain prostate changes**: Men with cells called high-grade *prostatic intraepithelial neoplasia* (PIN) may be at increased risk of prostate cancer. These prostate cells look abnormal under a microscope.
  - **Certain *genome* changes**: Researchers have found specific regions on certain *chromosomes* that are linked to the risk of prostate cancer. According to recent studies, if a man has a genetic change in one or more of these regions, the risk of prostate cancer may be increased. The risk increases with the number of genetic changes that are found. Also, other studies have shown an elevated risk of prostate cancer among men with changes in certain *genes*, such as *BRCA1* and *BRCA2*.

- **Symptoms of Prostate Cancer**

A man with prostate cancer may not have any symptoms. For men who do have symptoms, the common symptoms include:

Urinary problems

- Not being able to pass urine
- Having a hard time starting or stopping the urine flow
- Needing to urinate often, especially at night
- Weak flow of urine
- Urine flow that starts and stops

Pain or burning during urination
Difficulty having an *erection*
Blood in the urine or semen
Frequent pain in the lower back, hips, or upper thighs

Most often, these symptoms are not due to cancer. BPH, an infection, or another health problem may cause them. If you have any of these symptoms, you should tell your doctor so that problems can be diagnosed and treated.

- **Screening with Early Detection**

Your doctor can check for prostate cancer before you have any symptoms. During an office visit, your doctor will ask about your personal and family medical history. You'll have a physical exam. You may also have one or both of the following tests:

- *Digital rectal exam*: Your doctor inserts a lubricated, gloved finger into the rectum and feels your prostate through the rectal wall. Your prostate is checked for hard or lumpy areas.

- **Blood test for *prostate-specific antigen* (PSA)**: A lab checks the level of PSA in your blood sample. The prostate makes PSA. A high PSA level is commonly caused by BPH or *prostatitis* (*inflammation* of the prostate). Prostate cancer may also cause a high PSA level.

- **Treatment**

  a. Active Surveillance

b. Surgery
c. Radiation Therapy
d. Hormone Therapy
e. Chemotherapy

- **Risk Categories: Sporadic, Familial, vs. Putative Hereditary**

  Sporadic: what is normally expected in the general population; occurs at the same rate and around the same age
  Familial: cancer occurs more frequently within a family than what we would expect in the general population; usually occurs more than once among siblings
  Hereditary: cancer occurs much more frequently than expected in the general population and occurs in more than one generation

- **Genetic Testing with Counseling for future studies**
  a. Informed Consent to Store a DNA sample for Future Undefined Genetic Studies
  b. Benefits of Genetic Testing
  c. Risks of Genetic Testing
  d. Limitations of Genetic Studies
  e. How Genetic Information is handled by medical and life insurance companies; GINA law

- **Cardinal Features of Hereditary Syndrome**
  a. Cancer occurs at a much earlier age than seen in the general population; usually 10-20 years earlier
  b. Same type of cancer occurs more frequently within a single family
  c. Same type of cancer occurs in more than one generation in the family
  d. Same cancer occurs more than once in a single individual

Figure 4. Kaplan-Meier analysis of familiality using definition 1 (any first degree relatives plus nephews affected with prostate cancer).

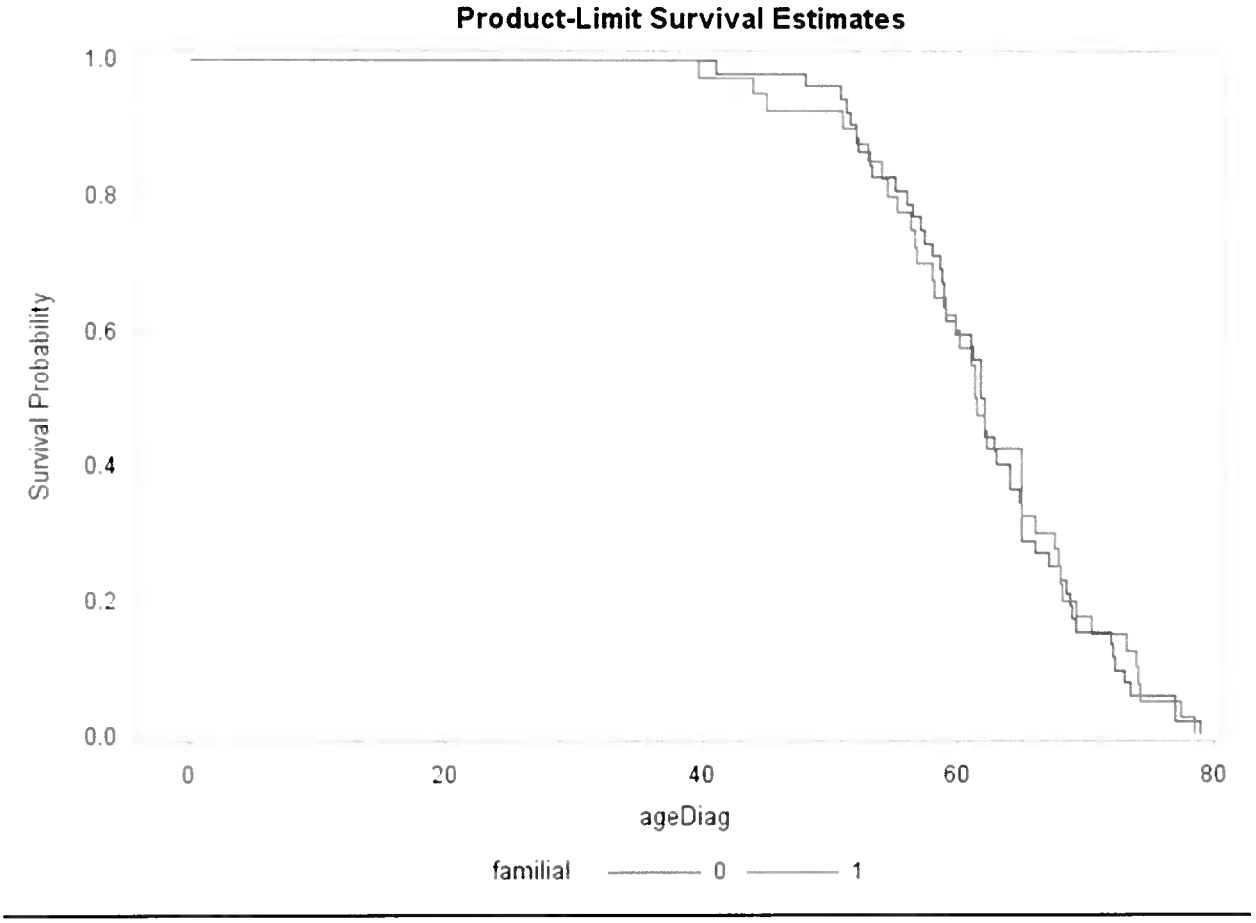

Figure 5. Kaplan-Meier analysis of familiality using definition 2 ((any first degree relatives plus nephews and/or cousins affected with prostate cancer).

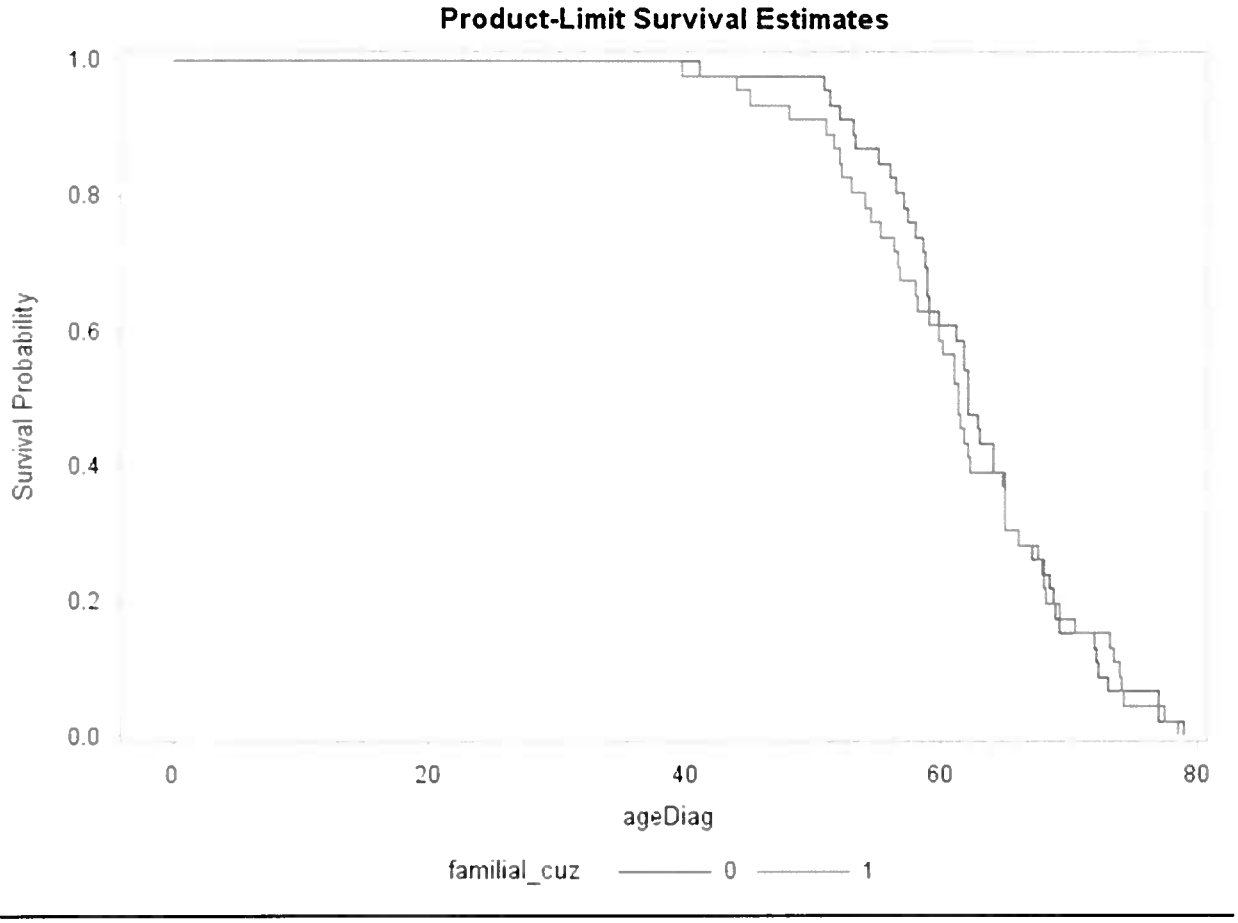

Figure 6. Kaplan-Meier analysis of familiality using definition 1 (any first degree relatives plus nephews affected with prostate cancer), JSU only.

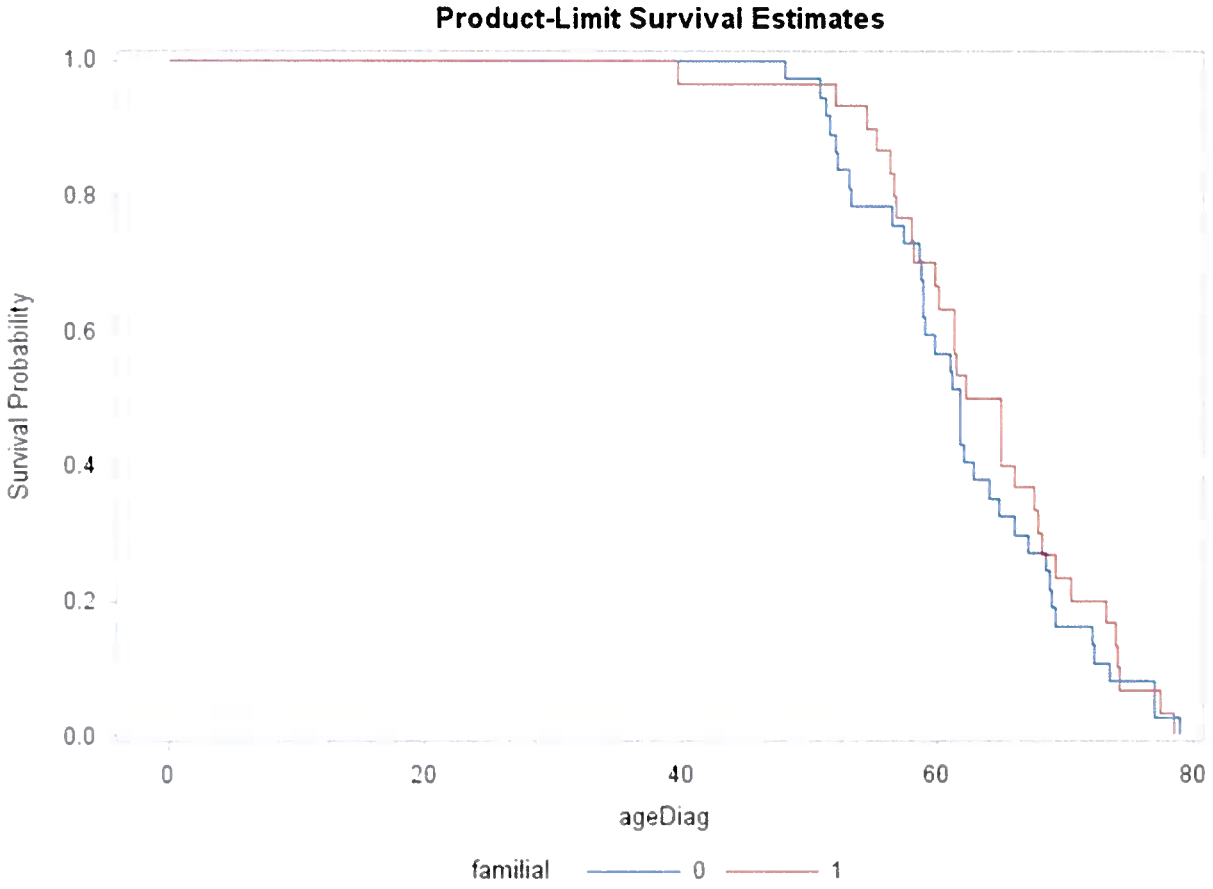

Figure 7. Kaplan-Meier analysis of familiality using definition 1 (any first degree relatives plus nephews affected with prostate cancer), CU only.

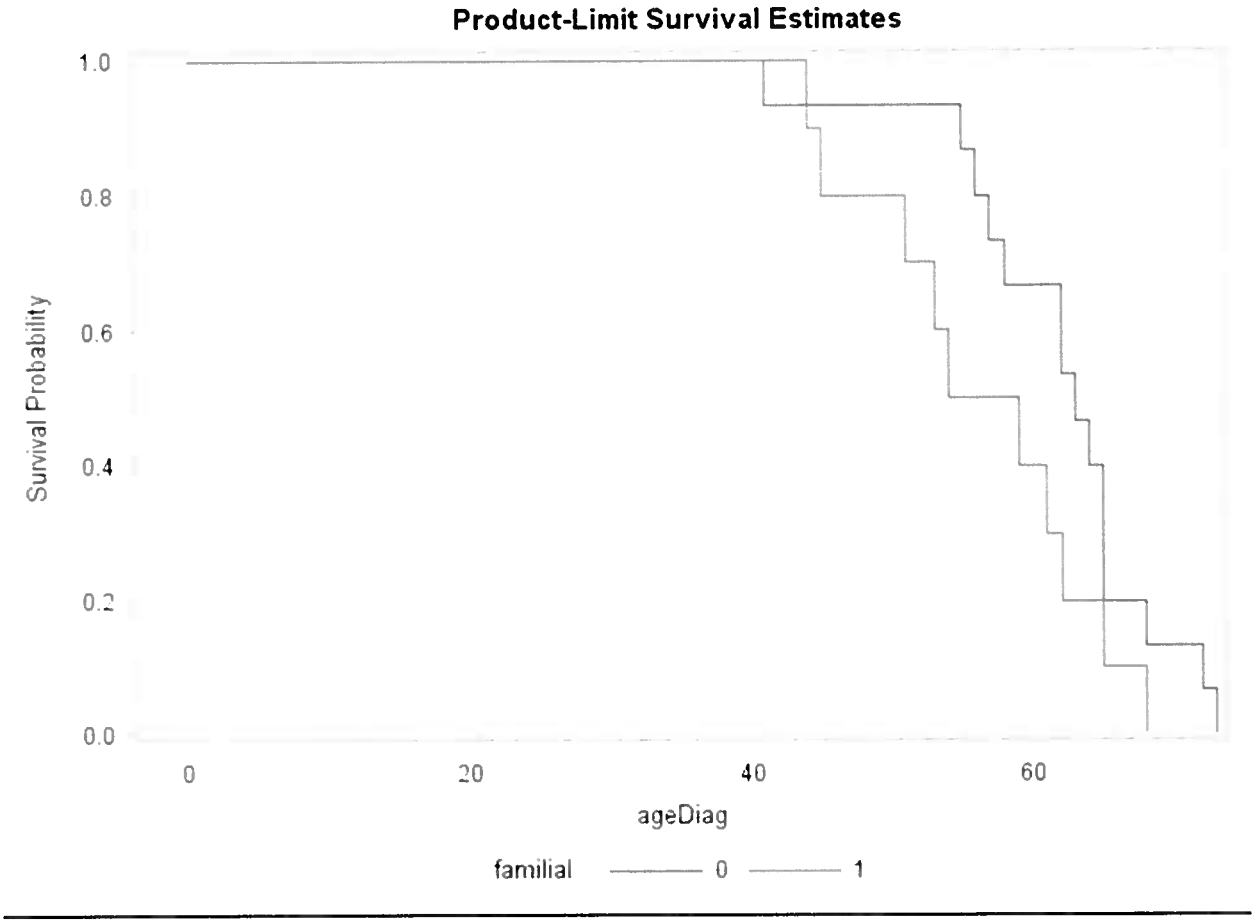

Figure 8. Kaplan-Meier analysis of familiality using a stricter definition (2 first degree affected relatives in addition to an affected individual), CU only.